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| RESULT | OK |

Attorney's Docket No.: 08952-008001
Client's Ref. No.: UMA 00-19

# OFFICIAL COMMUNICATION

# FACSIMILE

# FOR THE PERSONAL ATTENTION OF:

# EXAMINER VANESSA L. FORD

# UNITED STATES PATENT AND TRADEMARK OFFICE

# COMMISSIONER FOR PATENTS

# WASHINGTON, D.C. 20231

## GROUP 1645 FAX NO: (703) 308-4242

**Number of pages including this page** 19

Applicant : Elizabeth S. Stuart et al.
Serial No. : 09/827,490
Filed : April 6, 2001

Art Unit : 1645
Examiner : Vanessa L. Ford

FACSIMILE COMMUNICATION

Title : CHLAMYDIAL GLYCOLIPID VACCINES

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

Attached to this facsimile communication cover sheet are a Petition for Three-Month Extension of Time, Reply to Final Office Action Dated May 16, 2003, and Notice of Appeal, faxed this 14th day of November, 2003, to Group 1645, the United States Patent and Trademark Office.

Respectfully submitted,

Attorney's Docket No.: 08952-008001
Client's Ref. No.: UMA 00-19

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Respectfully submitted,

Date:November 14, 2003

J. Peter Fasse
Reg. No. 32,983

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Fax: (617) 542-8906

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION FOR THREE-MONTH EXTENSION OF TIME

Pursuant to 37 CFR §1.136, applicants hereby petition that the period for response to the action dated May 16, 2003, be extended for three months to and including November 17, 2003, November 16, 2003 being a Sunday.

Please apply the amount of $475 for the required extension of time fee, along with any other charges or credits, to Deposit Account No. 06-1050, referencing Attorney Docket No. 08952-008001.

Respectfully submitted,

Date: November 17, 2003

J. Peter Fasse
Reg. No. 32,983

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Boston, MA 02110-2804
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20756335.doc

CERTIFICATE OF TRANSMITTAL BY FACSIMILE

I hereby certify under 37 CFR §1.8(a) that this correspondence is being transmitted via facsimile on the date indicated below and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

November 14, 2003
Date of Deposit

Lisa G. Gray
Signature

Lisa G. Gray
Typed or Printed Name of Person Signing Certificate

Attorney's Docket No.: 08952-008001 / UMA 00-19

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No. : 09/827,490
Filed : April 6, 2001
Title : CHLAMYDIAL GLYCOLIPID VACCINES

Art Unit : 1645
Examiner : Vanessa L. Ford

**MAIL STOP AF**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NOTICE OF APPEAL

Applicants hereby appeal to the Board of Patent Appeals and Interferences from the action dated May 16, 2003, finally rejecting claims 7-10, 15, 18 and 19.

A petition under 37 CFR §1.136 to extend the time to respond to the final rejection for three months to and including November 17, 2003 (November 16, 2003 being a Sunday), is enclosed.

Please apply the amount of $165 for the appeal fee, along with any other charges or credits, to Deposit Account No. 06-1050, referencing Attorney Docket No. 08952-008001.

Respectfully submitted,

Date: November 14, 2003

J. Peter Fasse
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20756358.doc

CERTIFICATE OF TRANSMITTAL BY FACSIMILE

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November 14, 2003
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Elizabeth S. Stuart et al.
Serial No. : 09/827,490
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Art Unit : 1645
Examiner : Vanessa L. Ford

**MAIL STOP AF**
Commissioner for Patents
P.O. Box 1450
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REPLY TO FINAL OFFICE ACTION DATED MAY 16, 2003

Please amend the above-identified application as follows:

CERTIFICATE OF TRANSMITTAL BY FACSIMILE

I hereby certify under 37 CFR §1.8(a) that this correspondence is being transmitted via facsimile on the date indicated below and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

November 14, 2003
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Lisa G. Gray
Signature

Lisa G. Gray
Typed or Printed Name of Person Signing Certificate

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1 to 6 (Canceled)

7. (Presently Amended) A composition comprising a carrier group covalently coupled to an ~~oligosaccharide obtained from a~~ isolated chlamydial glycolipid oligosaccharide.

8. (Presently Amended) The composition of claim 7, wherein the chlamydial glycolipid oligosaccharide is a GLXA oligosaccharide.

9. (Original) The composition of claim 7, wherein the carrier group is coupled to the oligosaccharide by a linker.

10. (Original) The composition of claim 9, wherein the linker is 2-(4-aminophenyl)ethylamine.

11 to 14 (Canceled)

15. (Presently Amended) A ~~purified~~ preparation consisting essentially of purified chlamydial glycolipid exoantigen, ~~wherein the preparation is free of other components~~ as determined by sodium dodecylsulfate gel electrophoreses and silver staining.

16 and 17 (Canceled)

18. (Presently Amended) A composition comprising a carrier group covalently coupled to an isolated chlamydial glycolipid oligosaccharide, wherein the oligosaccharide is capable of binding anti-GLXA monoclonal antibody 89MS30.

19. (Previously Presented) The composition of claim 7, wherein the carrier group is selected from the group consisting of bovine serum albumin (BSA); tetanus toxoid; Diphtheria CRM 197 Protein (CRM 197); ovalbumin; and an organic polymer.

## REMARKS

Claims 7 to 10, 15, 18, and 19, are pending in this application. Applicants thank Examiners Ford and Minnifield for their time to conduct a telephone interview on October 22, 2003. The pending claims and potential amendments were discussed. The amendments proposed herein seek to revise the claims along the lines discussed during the interview. Specifically, applicants propose to amend claims 7 and 18 to recite a composition comprising a carrier group covalently coupled to an isolated chlamydial glycolipid oligosaccharide. Claim 8 would be amended to recite that the chlamydial glycolipid recited in claim 7 is a chlamydial glycolipid exoantigen (GLXA). Support for these amendments can be found throughout the specification, e.g., at page 1, lines 24 to 27, and at page 8, lines 12 to 17. Applicants propose to amend claim 15 to recite a preparation consisting essentially of purified GLXA, as determined by sodium dodecylsulfate (SDS) gel electrophoreses and silver staining. General support for this amendment can be found throughout the application. These amendments would add no new matter.

In addition, although the amendments set forth above would add several terms to the claims, they would raise no new issues that would require further consideration and/or search. Each of the terms to be added is well understood in the relevant field and is supported by the specification. Applicants submit that this amendment would place the claims into condition for allowance, or at least present the rejected claims in better form for consideration on appeal, and should therefore be entered after the final rejection under 37 C.F.R. § 1.116 (a).

### 35 U.S.C. § 102

Claim 15 remains rejected as allegedly anticipated by Stuart et al. (*Immunology*, 68:469-473 (1989)). During the interview, applicants' representative explained why the composition described in Stuart is not the same as that claimed by applicants. Specifically, applicants' representative reiterated applicants' point that the preparations described in Stuart include GLXA and a mixture of contaminating materials (a shortcoming acknowledged by Stuart itself at page 472, right column, lines 28 to 35), whereas the preparation of GLXA recited in claim 15 is

purified and free of other components. The superior purity of the claimed preparation is made possible through applicants' improved methods for isolating chlamydial glycolipids, which are described throughout the specification, e.g., at page 2, lines 10 to 20.

As discussed during the interview, applicants propose to amend claim 15 to further clarify the language used in the claim. Specifically, claim 15 as amended would recite that the preparation consists essentially of purified GLXA as determined by SDS gel electrophoreses and silver staining. Amended claim 15 would make clear that the preparation is free of other contaminating components, such as non-GLXA glycolipids (e.g., host cell glycolipids), that are present in prior art preparations. Applicants submit that the purified nature of the preparation is a basic and novel characteristic of the invention, which is made clear throughout the specification, e.g., at page 2, lines 21 to 27.

In addition, as request by Examiner Ford, applicants submit herewith a declaration signed by one of the co-inventors of the present application, Dr. Lloyd Semprevivo, under 37 C.F.R. § 1.132 ("the Semprevivo Declaration"), which provides a side-by-side comparison of the preparations described in Stuart and the preparation recited in claim 15. In his declaration, Dr. Semprevivo compares the GLXA isolation methods described in Stuart with those described in the present specification and provides chromatograms showing that the presently claimed GLXA preparation (Fig. 2) contains substantially fewer contaminants than Stuart's preparations (Fig. 1). As Dr. Semprevivo notes, "this protocol [described in the present application] results in a GLXA composition that is significantly better defined than those obtained using the previous protocol" (Declaration at para. 5). Applicants note that Fig. 3 is a Western blot of the silver stained gel in Fig. 2, which merely confirms that the two bands in the gel at about 32 and 62 kDa are GLXA.[1]

In view of the above, applicants respectfully request that the amendments to claim 15 be entered and that the present rejection be reconsidered and withdrawn.

Claims 7 to 9 remain rejected, and claim 18 is newly rejected, as allegedly anticipated by MacDonald et al. (U.S. Patent No. 5,716,793). During the interview, applicants' representative

[1] Applicants include an extra copy of the figures with this response, because the signed Declaration submitted with this response is a facsimile of a facsimile, which has lost much of its resolution. The original Declaration will be submitted by mail.

explained why the immune complex described in MacDonald is not the same as the oligosaccharide/carrier group conjugates recited in claims 7 to 9 and 18. Applicants respectfully maintain here that MacDonald does not anticipate the pending claims but, in the interests of moving the present application towards allowance, propose to amend claims 7, 8, and 18, as discussed in further detail below.

Reiterating applicants' previous argument (presented to Examiner Ford in applicants' previous Reply to the Office Action dated March 26, 2002, and during the telephone interview), applicants submit that MacDonald does not anticipate claims 7 to 9 and 18, because the immune complex described in McDonald at column 14, lines 34 to 40, includes whole GLXA, not an isolated oligosaccharide. The pending claims, on the other hand, recite compositions that include isolated oligosaccharide(s), not whole GLXA including such an oligosaccharide(s), coupled to a carrier group. Because McDonald does not disclose all of the elements of claims 7 to 9 and 18, MacDonald does not anticipate these claims.

In particular, MacDonald does not anticipate claims 7, 8, and 18, because MacDonald does not disclose an isolated oligosaccharide. In addition, as discussed in further detail below, MacDonald does not anticipate these claims because it does not describe a "carrier group," as defined in the specification. Accordingly, McDonald does not anticipate claims 7, 8, and 18, because it does not disclose all elements recited in those claims.

In particular, MacDonald does not anticipate claim 9 for the reasons discussed above with respect to claims 7, 8, and 18, and further because MacDonald does not disclose the linker recited in claim 9. Applicants note that the Office Action states (at page 4, item 4):

> The linker used to couple the carrier group to the oligosaccharide would be inherent in the teachings of the prior art.

However, as discussed during the interview, applicants respectfully disagree. The specification describes the recited linker by stating (at page 7, lines 21 to 25): "[a]ny standard chemical linker (e.g., a bi-functional linker containing, for example, reactive amino groups) can be used to couple the oligosaccharides to the carrier group. Examples of such linkers include 1-cyano-4-dimethylaminopyridinium tetrafluoroborate, 4-(4-N-maleimidomethyl)cyclohexane-1-

carboxyl hydrazide, and a phenethylamine-isothiocyanate derivative." Applicants submit that MacDonald does not describe, or even suggest, such linkers, or their use to couple isolated oligosaccharides to carriers. Therefore, MacDonald does not inherently disclose such linkers, and cannot anticipate claim 9.

Finally, even if the claims were somehow construed to cover whole GLXA coupled to a carrier group (i.e., a GLXA/carrier group conjugate), which they do not, MacDonald would still not anticipate the claims because MacDonald does not describe such a conjugate. This shortcoming becomes apparent upon closer inspection of MacDonald. In particular, the Office Action states (at page 4, item 4):

> MacDonald et al teach a covalently bound immune complex comprising paramagnetic particles (i.e. carrier group), GLXA, GLXA-antibody and GLXA-antibody labeled monoclonal GLXA-antibody IgG) (column 14, lines 34-40).

Based on the above, applicants believe the Office has interpreted the term "carrier group" to include paramagnetic particles. However, applicants' specification indicates (at page 7, lines 14 to 18) that a carrier group is a compound that "enhance(s) presentation of oligosaccharide epitopes to a mammalian immune system." The Office Action provides no evidence that suggests that a paramagnetic particle would enhance presentation of oligosaccharide epitopes to an immune system. Applicants submit that a paramagnetic particle does not fall within applicants' definition of a "carrier group."

Further, applicants believe the Office has interpreted MacDonald's shorthand recitation of the immune complex ("paramagnetic particles-GLXA-GLXA-Ab1-AE labeled monoclonal GLXA-Ab1 IgG" at column 14, lines 36-38) to indicate that MacDonald's paramagnetic particles are somehow directly bound to GLXA. However, a closer inspection of MacDonald reveals that this interpretation is incorrect. MacDonald states (at column 14, lines 33 to 36, immediately preceding MacDonald's shorthand recitation; emphasis added):

> Then, *polyclonal anti-chlamydial antibodies which were covalently bound to paramagnetic particles* (500 ul) was added to each tube and incubated for another hour.

From the above-quoted sentence, it is clear that the paramagnetic particles described in MacDonald as being part of the immune complex are covalently bound to anti-chlamydial antibodies, which, in turn, are bound to GLXA. Accordingly, any skilled practitioner would recognize that the phrase "paramagnetic particles-GLXA-GLXA-Ab1-AE labeled monoclonal GLXA-Ab1 IgG" is MacDonald's shorthand way of indicating that the immune complex includes a paramagnetic particle covalently bound to anti-chlamydial antibodies, which antibody is in turn bound (i.e., by typical antigen/antibody binding forces, e.g., hydrogen bonds, and electrostatic, van der Waals, and hydrophobic forces) to GLXA, which in turn, is bound to a labeled monoclonal antibody.

Thus, contrary to what is stated in the Office Action, MacDonald does not describe a carrier group covalently bound to GLXA but, rather, an immune complex that includes a paramagnetic particle covalently bound to an antibody which, in turn, is bound to GLXA by typical antigen/antibody binding forces.

Applicants submit, and the Office Action appears to confirm, that the pending claims would need to read on whole GLXA/carrier conjugates and the interpretations discussed above would have to be correct for MacDonald to anticipate these claims. However, as discussed above, neither condition is true. Accordingly, applicants submit that MacDonald does not anticipate claims 7 to 9 and 18.

However, in the interests of moving the present application towards allowance, and as discussed during the interview, applicants propose to amend claim 7 and 18 to recite a composition comprising a carrier group covalently coupled to an isolated chlamydial glycolipid oligosaccharide. The language of claim 8 would be amended to comport with that recited in claim 7. Applicants submit that amending the claims in this way would further clarify that applicants claim isolated chlamydial glycolipid oligosaccharide(s) covalently coupled (i.e., coupled directly or through a linker) to a carrier group, not an immune complex that includes whole GLXA, which is described in MacDonald. Because McDonald does not disclose the oligosaccharide/carrier group conjugates recited in claims 7 to 9 and 18 so amended, McDonald would not anticipate these claims.

For the reasons discussed above, applicants respectfully request that the proposed amendments to claims 7, 8, and 18, be entered and that the present rejection of claims 7 to 9 and 18 be reconsidered and withdrawn.

35 U.S.C. § 103

Claims 7 to 10 remain rejected, and claims 18 and 19 are newly rejected, as allegedly obvious over MacDonald et al. (U.S. Patent No. 5,716,793) in view of Smith et al (*J. Biol. Chem.* 255(1):55-59 (1980)). In response, applicants respectfully maintain that the claims are not obvious in view of MacDonald and Smith for the reasons stated in applicants' Response to Office Action filed March 3, 2003, and for the reasons stated below.

In maintaining the rejection, the Office Action states (at pages 6 and 7, item 5):

> It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention.
>
> * * *
>
> Applicant is arguing limitations that are not in the claims with their assertion that "Smith does not teach a method to prepare a GLXA component for derivatization by using trifluoracetolysis [sic]". It should be remembered that the claims are drawn to a composition which is a product and not a method. There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

As discussed during the interview, applicants submit that the last sentence of the above quoted language of the Office Action misstates the legal standard for finding that a combination of references renders an invention obvious. In fact, the proper standard is set out, for example, in the Manual of Patent Examining Procedure (MPEP) § 2143, which states:

> The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done. 'To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the

claimed invention to have been obvious in light of the teachings of the references.' *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).

Thus, the standard is not that there be some evidence showing that the combination of references would not suggest the claimed invention. Such a standard would easily be met under many circumstances. Rather, the true standard requires that the references themselves suggest the claimed invention or, alternatively, that the examiner present convincing arguments as to why the invention is obvious in view of the teachings of the references. Applicants respectfully submit that the correct standard has not been met in this case.

Further, contrary to the Office Action's above-quoted assertions, applicants respectfully submit that they have, in fact, clearly addressed the previous Office Action's cited combination of references. Applicants were not arguing unclaimed limitations, but were explaining that Smith and MacDonald provided skilled practitioners with no motivation to combine these two references. In making their arguments, applicants were explaining why the previous Office Action failed meet the true standard discussed above, i.e., why the Office Action failed to establish a *prima facie* case of obviousness.

Naturally, as a first step, applicants discussed the shortcomings of MacDonald and Smith individually. MacDonald describes methods for detecting chlamydia in biological samples, e.g., by contacting biological samples with GLXA-$Ab_1$ or – $Ab_3$ to detect GLXA in a sample. McDonald does not disclose isolated oligosaccharides obtained from this chlamydial glycolipid, and does not even suggest that useful individual oligosaccharides should be (or could be) cleaved from GLXA, or chemically synthesized based upon these oligosaccharides. Accordingly, MacDonald could not disclose or suggest that such isolated oligosaccharide(s) could be coupled to a carrier, nor could it suggest methods for performing such coupling.

With respect to Smith, applicants explained that it does not provide the information missing in MacDonald. Smith describes a method for derivatizing free oligosaccharides from human milk for coupling to proteins, and the use of such oligosaccharide-protein conjugates to generate immune responses in rabbits. Smith does not disclose chlamydial glycolipids such as GLXA. Further, Smith does not even suggest that Smith's methods could have been utilized

with whole glycolipids from prokaryotes of the genus *Chlamydia*, or for that matter, any other prokaryotic organism.

Next, as a second step, applicants explained that skilled practitioners would find no suggestion or motivation in MacDonald and Smith to combine these two references. Neither publication suggests that useful oligosaccharides could, or should have been isolated from chlamydial glycolipids such as GLXA, or that they could have been coupled to carriers using the methods taught in the present application. Thus, a skilled practitioner would not have been motivated by Smith to modify the methods described in McDonald to create the compositions recited in claims 7 to 10, 18, and 19.

With respect to the requisite reasonable expectation of success, applicants explained that even if MacDonald's whole GLXA were somehow treated using the method and linker described in Smith (i.e., if MacDonald and Smith were somehow combined), the claimed compositions still would not have been obtained. This is the case, in part, because GLXA and other commonly occurring glycolipids do not, as part of the native molecule, contain reducing ketone or aldehyde groups. Thus, to prepare a GLXA component for derivatization, it must first be subjected to trifluoroacetolysis to develop such a group(s) (see, e.g., the specification at page 15, line 28, to page 16, line 2). Smith does not disclose, or even suggest, treating glycolipids using trifluoracetolysis to develop such groups. Therefore, even if the methods described in Smith were used to treat GLXA, applicants' claimed compositions would not have been obtained.

Applicants submit that neither of the publications cited in the Office Action, singly or in combination, suggested developing the compositions of the present invention.

Accordingly, applicants submit that they have, in fact, thoroughly addressed the Office's cited combination of MacDonald and Smith and that the Office Action has not established that the claims are obvious over this combination. Thus, applicants request that the present rejection be reconsidered and withdrawn.

35 U.S.C. § 112, First Paragraph

Claim 18 was rejected for an alleged lack of enablement because, according to the Office Action, applicants must provide evidence that a biological deposit of antibody 89MS30 has been made. Applicants respectfully submit that 89MS30 was described in U.S. Patent No. 5,840,297, which indicates (at column 9, lines 18 to 20) that the hybridoma cell line producing this monoclonal antibody was deposited with the American Type Culture Collection (ATCC) as ATCC H.B. 11300. Further, as discussed during the interview, applicants provide herewith a copy of the ATCC deposit receipt (attached hereto as "Exhibit A") acknowledging that the 89MS30-producing hybridoma was deposited on March 12, 1993. Thus, applicants respectfully request that this rejection be reconsidered and withdrawn.

## CONCLUSION

Applicants request that the proposed claim amendments be entered, and submit that all of the claims as amended would be in condition for allowance, which actions are requested. A Petition for a Three-Month Extension of Time is enclosed. Please apply a fee of $475 for the extension to Deposit Account No. 06-1050, referencing Attorney Docket Number 08952-008001.

Respectfully submitted,

Date: November 14, 2003

J. Peter Fasse
Reg. No. 32,983

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Attorney's Docket No.: 08952-008001 / UMA 00-19

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Art Unit : 1645
Examiner : Vanessa L. Ford

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

## DECLARATION UNDER 37 C.F.R. § 1.132

I, Lloyd Semprevivo, declare that:

1. I am a co-inventor of the subject matter claimed in the patent application captioned above ("the present application").

2. I understand that claim 15 of the present application has been rejected by the U.S. Patent & Trademark Office Examiner in a final Office Action dated May 16, 2003, as allegedly anticipated by Stuart et al. (*Immunology*, 68:469-473 (1989)). I have reviewed this reference. According to the Office Action, Stuart discloses purified chlamydial glycolipids that are free of other components as determined by sodium dodecylsulfate gel electrophoresis and silver staining. Further, the Office Action indicates that applicants should provide a side-by-side comparison to show that the preparation recited in claim 15 is different from those disclosed in Stuart.

3. The present declaration provides the side-by-side comparison requested in the Office Action. Specifically, Figs. 1 to 3, below, show the significant progression in methodology for

isolating GLXA from infected culture supernatants and provide silver stained gels of the preparations. Note that Fig. 1, below, is a duplicate of Stuart's Fig. 2.

4. Fig. 1 is a picture of a silver stained 8-25% SDS-PAGE PhastGel™ of GLXA purified from the supernatant of cultures infected with different serovars of chlamydia [lanes a-d]. Molecular weight standards are included [lane e]. This figure (reproduced from Stuart) illustrates the purity of preparations obtained using early methodology involving Octyl-Sepharose hydrophobic chromatography to initially isolate antigen, followed by re-isolation of 'shifted' GLXA using potassium thiocyanate (KSCN) and Octyl-Sepharose. Note that when the polyclonal antibody is used, other chlamydial components are isolated from the culture media, along with GLXA. As a result, lanes a to d show many bands, indicating that a substantial amount of contaminating materials is present along with the GLXA.

5. Figs. 2 and 3 are pictures of a silver stained gel and a Western blot, respectively, illustrating results obtained using the protocol described in the present application. In the protocol, supernatants from infected cultures are ultracentrifuged and subjected to DNAse, RNAse, and mAb1 affinity column treatment, as described in the specification, e.g., at page 2, lines 10 to 20. Clearly, this protocol results in a GLXA composition that is significantly better defined than those obtained using the previous protocol. Samples were analyzed by electrophoresis using an 8-16% Tris-Glycine pre-cast Novex™ gel. Aliquots were electrophoresed and then transferred to polyvinylidene fluoride (PVDF) membrane and immuno-probed using monoclonal antibody (89MS30) (see Fig. 3). In Fig. 2 and Fig. 3, GLXA appears as the bands having molecular weights of about 62 kDa and 32 kDa (the 32 kDa band is likely a fragment or subunit of the 62 kDa band). This product can subsequently be used to generate the isolated oligosaccharides described in the present application.

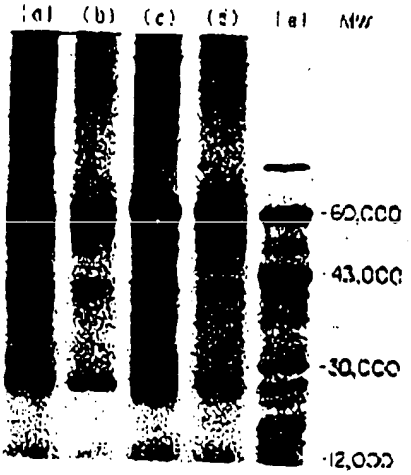


Fig. 1

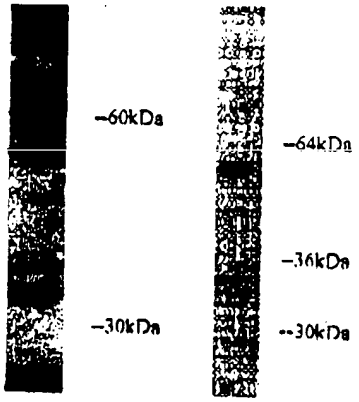


Fig. 2 Fig. 3

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 13 Nov 03

Lloyd H. Semprevivo, Ph.D.

20750423.doc

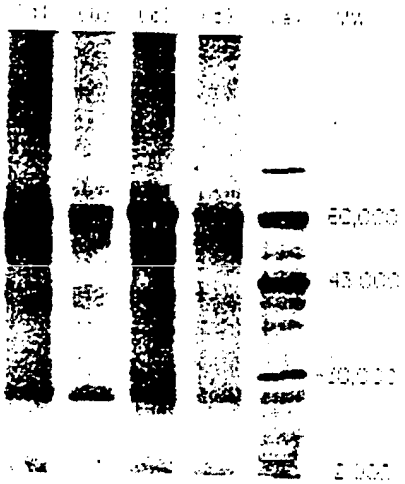

Fig. 1

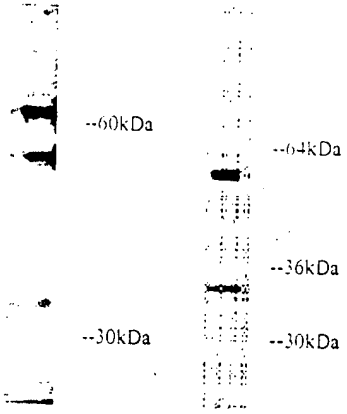


Fig. 2




Fig. 3

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date:_____

_____

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